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TCACCAGGTGCTCACCTTCCTCCTGCTCTTCGTGATCACCTCGGTGGCCTCTGAAAACGCCAGCACATCC
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TCTGGGGCGTCTCTTTGCGCTCTGCTTCTCCTGCCTGCTGAGCCAGGCATGGCGCGTGCGGAGGCTGGT
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CTCATCTGGGTGGCCTGGATGACCATGTACCTCTTCGGCAATGTCAAGCTGCAGCAGGGGGATGCCTGGA
ACGACCCACCTTGGCCATCACGCTGGCGGCCAGCGGCTGGGTCTTCGTCTATCTTCCACGCCATCCCTGA
GATCCACTGCACCCTTCTGCCAGCCCTGCAGGAGAACACGCCCAACTACTTCGACACGTGCGAGCCCAGG
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CAGCTTGGGAAAAAGACCCAGCGCTCCGTTTAGAAGCAACGTGTATCAGCCAACTGAGATGGCCGTCGTG
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GAAATGTGGCTGGGAAGACTGTTTCATCCTCTGGGGGTAGAACAGAACCAAATTCACAGCTGGTGGGCC
AGACTGGTGTGTTGGTGGAGGTGGGGGGCTCCCACTCTTATCACCTCTCCCCAGCAAGTGCTGGACCCAG
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CGTGGGGTGAGCTTTATAGCCAGTAGAGGTGGAGGGACCCTGGCATGTGCCAAAGAAGAGGCCCTCTGGG
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TTAACCTTTAAAGAAAAATGAAAAGGTTAGTGTTTGGGGGCCGGGGGAGGACTGACCGCTTCATAAGCC
AGTACGTCTGAGCTGAGTATGTTTCAATAAACCTTTTGATATTTCTCAAAAAAAAAAAAAAAAAAAAAA
(SEQ ID NO:1)

FIGURE 1A

MFVASERKMRAHQVLTFLLLFVITSVASENASTSRGCGLDLLPQYVSLCDLDAIWGIVVEAVAG
AGALITLLMLILLVRLPFIKEKEKKSPVGLHFLFLLGTLGLFGLTFAFIIQEDETICSVRRFL
WGVLFALCFSCLLSQAWRVRRLVRHGTGPAGWQLVGLALCLMLVQVIIAVEWLVLTVLRDTRPA
CAYEPMDFVMALIYDMVLLVVTGLGLALFTLCGKFKRWKLNGAFLITAFLSVLIWVAWMTMYLF
GNVKLQQGDAWNDPTLAITLAASGWVFVIFHAIPEIHCTLLPALQENTPNYFDTSQPRMRETA
EEDVQLPRAYMENKAFSMDEHNAALRTAGFPNGSLGKRPSGSLGKRPSAPFRSNVYQPTEMAVV
LNGGTIPTAPPSHTGRHLW (SEQ ID NO:2)

FIGURE 1B

underlined = deleted in targeting construct

bold = sequence flanking Neo insert in targeting construct

AGGTCGCAGGCGGGCGTGCGTGGAGCGGGGGCGCGGGCGCGCCGAGAGATGTGACTCG
 GGCCGAAGGCCAGCTGGAGCGTCCGGCGTCCGGGGCGCGGGGGT**CGAATGTTCTGTGGCA**
TCAGAGAGAAAGATGAGAGCTCACCAGGTGCTCACCTTCCTCCTGCTCTTCGTGATCACC
TCGGTGGCCTCTGAAAACGCCAGCACATCCCAGGCTGTGGGCTGGACCTCCTCCCTCAG
TACGTGTCCCTGTGCGACCTGGACGCCATCTGGGGCATTGTGGTGGAGGCGGTGGCCGGG
GCGGGCGCCCTGATCACACTGCTCCTGATGCTCATCCTCCTGGTGGGCTGCCCTTCATC
AAGGAGAAGGAGAAGAAGAGCCCTGTGGGCTCCACTTCTGTTCTCCTCCTGGGGACCCTG
GGCCTCTTTGGGCTGACGTTTGCCTTCATCATCCAGGAGGACGAGACCATCTGCTCTGTC
CGCCGCTTCCTCTGGGGCGTCTCTTTGCGCTCTGCTTCTCCTGCCTGCTGAGCCAGGCA
TGGCGCGTGCGGAGGCTGGTGGCGCATGGCACGGGCCCCGCGGGCTGGCAGCTGGTGGGC
CTGGCGCTGTGCTGATGCTGGTGCAAGTCATCATCGCTGTGGAGTGGCTGGTGTCTCACC
GTGCTGCGTGACACAAGGCCAGCCTGCGCCTACGAGCCCATGGACTTTGTGATGGCCCTC
ATCTACGACATGGTACTGCTTGTGGTCACCCTGGGGCTGGCCCTCTTCACTCTGTGCGGC
AAGTTCAGAGGTGGAAGCTGAACGGGGCCTTCCTCCTCATCACAGCCTTCCTCTCTGTG
CTCATCTGGGTGGCCTGGATGACCATGTACCTCTTCGGCAATGTCAAGCTGCAGCAGGGG
GATGCCTGGAACGACCCACCTTGGCCATCACGCTGGCGGCCAGCGGCTGGGTCTTCGTC
ATCTTCCACGCCATCCCTGAGATCCACTGCACCCTTCTGCCAGCCCTGCAGGAGAACACG
CCCACTACTTCGACACGTCCGAGCCAGGATGCGGGAGACGGCCTTCGAGGAGGACGTG
CAGCTGCCCGGGCCCTATATGGAGAACAAGGCCCTTCTCCATGGATGAACACAATGCAGCT
CTCCGAACAGCAGGATTTCCCAACGGCAGCTTGGGAAAAAGACCCAGTGGCAGCTTGGGG
AAAAGACCCAGCGCTCCGTTTAGAAGCAACGTGTATCAGCCAAGTGAATGGCCGTCGTG
CTCAACGGTGGGACCATCCCAACTGCTCCGCCAAGTCACACAGGAAGACACCTTTGGTGA
AAGACTTTAAGTTCAGAGAATCAGAATTTCTCTTACCGATTTGCCTCCCTGGCTGTGTC
TTTCTTGAGGGAGAAATCGGTAACAGTTGCCGAACAGGCCGCTTCACAGCCAGGAAATT
TGGAAATCCTAGCCAAGGGGATTTTCGTGTAAATGTGAACACTGACGAAGTAAAAGCTAA
CACCGACTGCCCCCCCCCTCCCTGCCACACACAGACACGTAATACCAGACCAACCTCA
ATCCCCGCAAACTAAAGCAAAAGCTAATTGCAAAATAGTATTAGGCTCACTGGAATGTGG
CTGGGAAGACTGTTTCATCCTCTGGGGGTAGAACAGAACCAATTCACAGCTGGTGGGCC
AGACTGGTGTGTGGTGGAGGTGGGGGGCTCCCACTCTTATCACCTCTCCCCAGCAAGTGC
TGGACCCCAAGTAGCCTCTTGGAGATGACCGTTGCGTTGAGGACAAATGGGGACTTTGCC
ACCGGCTTGCTTGGTGGTTTGCACATTTACAGGGGGTTCAGGAGAGTTAAGGAGGTGTGG
GTGGGATTTCAAGGTGAGGCCCAACTGAATCGTGGGGTGAGCTTTATAGCCAGTAGAGGT
GGAGGGACCTTGGCATGTGCCAAAGAAGAGGCCCTCTGGGTGATGAAGTGACCATCACAT
TTGGAAGTGATCAACCACTGTTCCCTTCTATGGGGCTCTTGCTCTAATGTCTATGGTGAG
AACACAGGCCCCGCCCTTCCCTTGTAGAGCCATAGAAATATTCTGGCTTGGGGCAGCAG
TCCCTTCTTCCCTTGATCATCTCGCCCTGTTCCCTACACTTACGGGTGTATCTCCAAATCC
TCTCCCAATTTTATCCCTTATTCATTTCAAGAGCTCCAATGGGGTCTCCAGCTGAAAGC
CCCTCCGGGAGGCAGGTGGAAAGGCAGGCACCACGGCAGGTTTTCGCGATGATGTCACC
TAGCAGGGCTTCAGGGGTTCCTACTAGGATGCAGAGATGACCTCTCGCTGCCTCACAAAGC
AGTGACACCTCGGGTCCCTTCCGTTGCTATGGTGAAAAATTCCTGGATGGAATGGATCACA
TGAGGGTTTCTTGTGCTTTTGGAGGGTGTGGGGGATATTTGTTTGGTTTCTGTCAG
GTTCCATGAAAACAGCCCTTTTCCAAGCCCATGTTTCTGTCTATGGTTTCCATCTGTCCCT
GAGCAAGTCATTCCTTTGTTATTTAGCATTTTGAACATCTCGGCCATTCAAAGCCCCAT
GTTCTCTGCACGTGTTTGGCCAGCATAACCTCTAGCATCGATTCAAAGCAGAGTTTAAACC
TGACGGCATGGAATGTATAAATGAGGGTGGGTCTTCTGCAGATACTCTAATCACTACAT
TGCTTTTCTATAAACTACCCATAAGCCTTTAACCTTTAAAGAAAAATGAAAAAGTTA
GTGTTTGGGGGCGGGGGAGGACTGACCGCTTCATAAGCCAGTACGCTGAGCTGAGTAT
GTTTCAATAAACCTTTTGATATTTCTCAAAAAAAAAAAAAAAAAAAAAA

FIGURE 2A

Gene Sequence
Structure *

526 bp

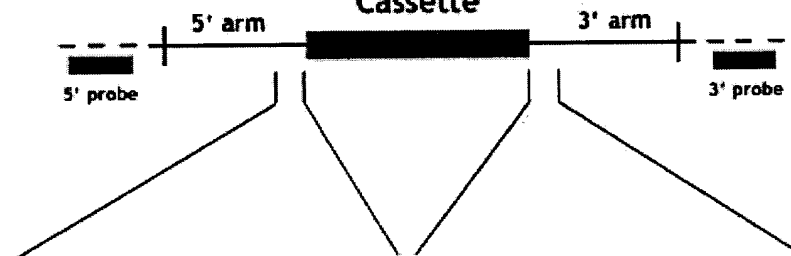
Sequence Deleted

594 bp

Size of full-length
cDNA: 2870 bp

Targeting Vector*
(genomic sequence)

LacZ-Neo
Cassette



Arm Length:
5': 4.2 kb
3': 0.7 kb

———— Targeting Vector
----- Endogenous Locus

* Not drawn to scale

5' >TGATGCTCATTCTCCTAGTGA
GACTACCC TTCATCAAGGACAAGG
AAAGGAAGCGGCTGTGTGCCTCC
ATTTCTCTTCC TGCTGGGGACCC
TGGGCCCTCTTTGGCCTGACGTTTG
CCTTCATCATCCAGATGGACGAGA
CAATCTGCTCCATCCGACGCTTCC
TCTGGGGTGTCTCTTCGCGCTCT
GCTTTTCCGCT <3' (SEQ ID
NO: 3)

5' >GTGAGCCTGGCACTGTGCCTG
ATGCTGGTGCAGGTCATCATTGCC
ACTGAGTGGCTGGTGCTGACTGTG
CTGCGTGACACGAAGCCAGCCTGC
GCCTACGAGCCCATGGATTTTGTG
ATGGCGCTCATCTACGACATGGTG
CTGCTGGCCATCACCTGGCCAG
TCCCTCTTACGCTGTGTGGCAAG
TTCAAACGGTG <3' (SEQ ID
NO: 4)

FIGURE 2B

Hot Plate Test

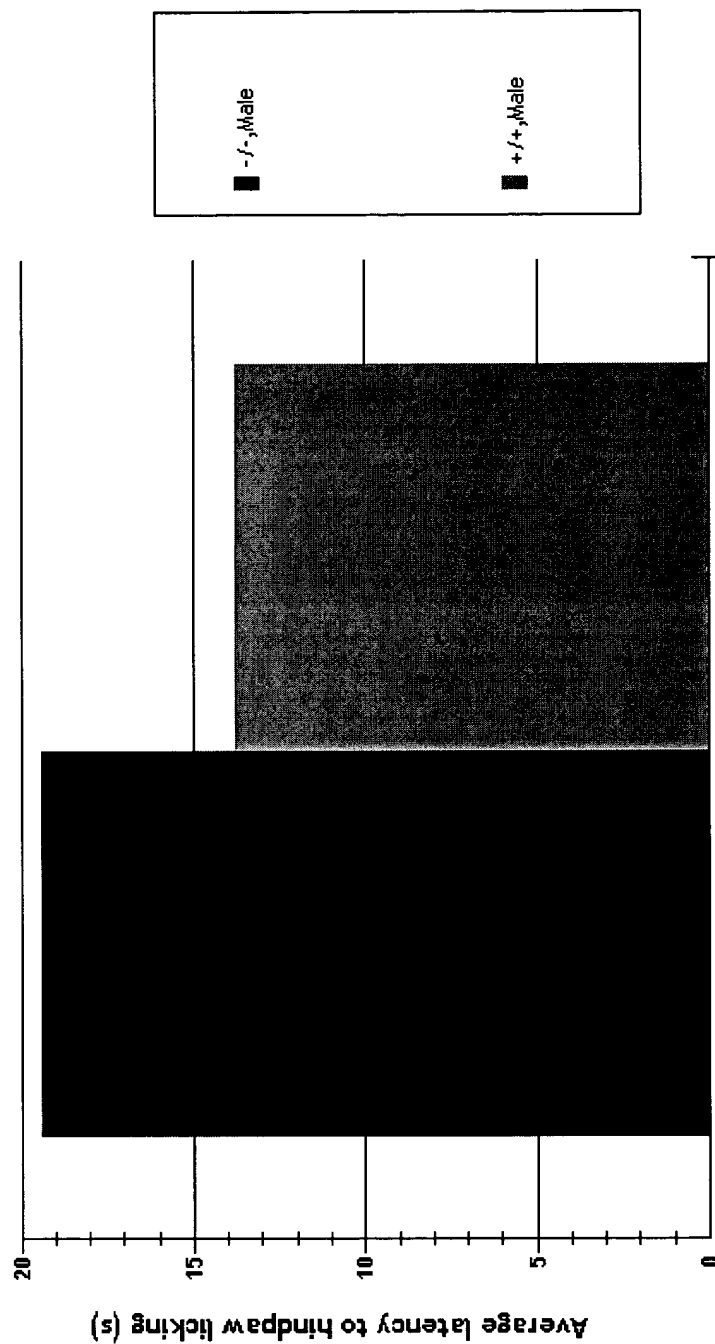


FIGURE 3